

10/554,271

## EAST Search History

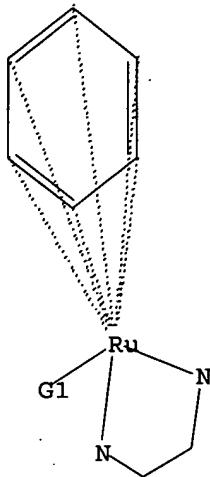
Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	707	(556/137).CCLS.	US-PGPUB; USPAT; EPO; JPO	OR	OFF	2007/03/04 17:29
L2	905	(514/492).CCLS.	US-PGPUB; USPAT; EPO; JPO	OR	OFF	2007/03/04 17:29

10/554,271

(FILE 'HOME' ENTERED AT 16:55:19 ON 04 MAR 2007)

FILE 'REGISTRY' ENTERED AT 16:55:42 ON 04 MAR 2007  
L1 STRUCTURE uploaded

=> d 11  
L1 HAS NO ANSWERS  
L1 STR



G1 O,S,N,Cl,Br,F,I

Structure attributes must be viewed using STN Express query preparation.

=> s 11  
SAMPLE SEARCH INITIATED 16:56:15 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 2475 TO ITERATE

80.8% PROCESSED 2000 ITERATIONS 28 ANSWERS  
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 46516 TO 52484  
PROJECTED ANSWERS: 340 TO 1046

L2 28 SEA SSS SAM L1

=> s 11 full  
FULL SEARCH INITIATED 16:56:25 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 49810 TO ITERATE

100.0% PROCESSED 49810 ITERATIONS 715 ANSWERS  
SEARCH TIME: 00.00.01

L3 715 SEA SSS FUL L1

=> fil caplus  
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL  
FULL ESTIMATED COST 172.10 SESSION 172.31

FILE 'CAPLUS' ENTERED AT 16:56:30 ON 04 MAR 2007

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FILE COVERS 1907 - 4 Mar 2007 VOL 146 ISS 11  
FILE LAST UPDATED: 2 Mar 2007 (20070302/ED)

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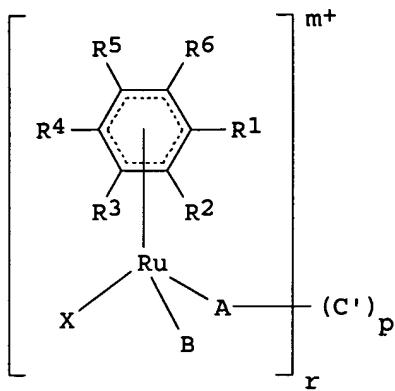
<http://www.cas.org/infopolicy.html>

=> s 13  
L4 221 L3  
  
=> s 14 and py<2004  
23916064 PY<2004  
L5 109 L4 AND PY<2004  
  
=> s 15 and cancer  
307771 CANCER  
L6 4 L5 AND CANCER  
  
=> d 1-4 bib abs  
  
L6 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN  
AN 2002:482176 CAPLUS  
DN 138:130575  
TI In vitro and in vivo activity and cross resistance profiles of novel ruthenium (II) organometallic arene complexes in human ovarian cancer  
AU Aird, R. E.; Cummings, J.; Ritchie, A. A.; Muir, M.; Morris, R. E.; Chen, H.; Sadler, P. J.; Jodrell, D. I.  
CS Cancer Research UK, Edinburgh Oncology Unit, Western General Hospital, Edinburgh, EH4 2XR, UK  
SO British Journal of Cancer (2002), 86(10), 1652-1657  
CODEN: BJCAAI; ISSN: 0007-0920  
PB Nature Publishing Group  
DT Journal  
LA English  
AB Ruthenium complexes offer the potential of reduced toxicity, a novel mechanism of action, non-cross resistance, and a different spectrum of activity compared to Pt containing compds. Thirteen novel Ru(II) organometallic arene complexes were evaluated for activity (in vitro and in vivo) in models of human ovarian cancer, and cross-resistance profiles established in cisplatin and multi-drug-resistant variants. A broad range of IC<sub>50</sub> values was obtained (0.5 to >100 μM) in A2780 parental cells with 2 compds. (RM175 and HC29) equipotent to carboplatin (6 μM), and the most active compound (HC11) equipotent to cisplatin (0.6 μM). Stable bi-dentate chelating ligands (ethylenediamine), a more hydrophobic arene ligand (tetrahydroanthracene) and a single ligand exchange center (chloride) were associated with increased activity. None of the 6 active Ru(II) compds. were cross-resistant in the A2780cis cell

line, demonstrated to be 10-fold resistant to cisplatin/carboplatin by a mechanism involving, at least in part, silencing of MLH1 protein expression via methylation. Varying degrees of cross-resistance were observed in the P-170 glycoprotein overexpressing multi-drug-resistant cell line 2780AD that could be reversed by co-treatment with verapamil. In vivo activity was established with RM175 in the A2780 xenograft together with non-cross-resistance in the A2780cis xenograft and a lack of activity in the 2780AD xenograft. High activity coupled to non cross-resistance in cisplatin resistant models merit further development of this novel group of anticancer compds.

RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6	ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN				
AN	2002:31461 CAPLUS				
DN	136:85944				
TI	Half-sandwich ruthenium(II) compounds comprising heteroatom containing ligands for treatment of cancer				
IN	Morris, Robert Edward; Sadler, Peter John; Jodrell, Duncan; Chen, Haimei				
PA	University Court, the University of Edinburgh, UK				
SO	PCT Int. Appl., 32 pp.				
	CODEN: PIXXD2				
DT	Patent				
LA	English				
FAN.CNT 1					
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002002572	A1	20020110	WO 2001-GB2824	20010626 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2414446	A1	20020110	CA 2001-2414446	20010626 <--
	EP 1294732	A1	20030326	EP 2001-945472	20010626 <--
	EP 1294732	B1	20040818		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001012122	A	20030513	BR 2001-12122	20010626 <--
	JP 2004502696	T	20040129	JP 2002-507824	20010626
	AT 273985	T	20040915	AT 2001-945472	20010626
	PT 1294732	T	20041231	PT 2001-945472	20010626
	ES 2227225	T3	20050401	ES 2001-1945472	20010626
	US 2004029852	A1	20040212	US 2003-312940	20030815
	US 6936634	B2	20050830		
PRAI	GB 2000-16052	A	20000630		
	WO 2001-GB2824	W	20010626		
OS	MARPAT 136:85944				
GI					



I

AB The preparation of compds. [I; wherein R1 and R2 together with the ring to which they are bound represent a saturated or unsatd. carbocyclic or heterocyclic group; R3, R4, R5, R6, independently = H, alkyl, aryl, alkaryl, or CO<sub>2</sub>R' (R' = alkyl, aryl, or alkaryl); X = halo, H<sub>2</sub>O, sulfoxyl, carboxyl, etc.; A and B, independently = O-donor, N-donor, or S-donor ligands, or halo; C' = (C<sub>1</sub>-C<sub>12</sub>)alkylene, optionally substituted in or on the alkylene chain, bound to two A groups; p = 0, 1 and r = 1 when p = 0 and r = 2 when p = 1; m = 0, 1] is described. Thus, 1,4,9,10-tetrahydroanthracene is reacted with RuCl<sub>3</sub>•3H<sub>2</sub>O to give 89% [(η<sub>6</sub>-C<sub>14</sub>H<sub>12</sub>)RuCl<sub>2</sub>]<sub>2</sub>, which was complexed with ethylenediamine (en) in the presence of NH<sub>4</sub>PF<sub>6</sub> to give 33% [(η<sub>6</sub>-C<sub>14</sub>H<sub>12</sub>)RuCl(en)]<sup>+</sup>PF<sub>6</sub><sup>-</sup>. Compds. I are useful as antitumor agents, exhibiting IC<sub>50</sub> values as high as 315μM against A2780 ovarian cancer cell line. Biol. data are given.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

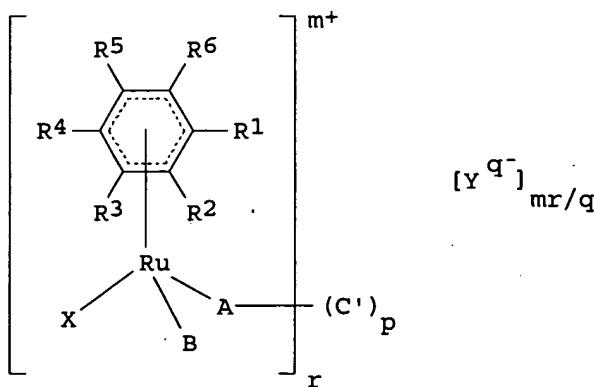
L6 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN  
AN 2001:719202 CAPLUS  
DN 136:15044  
TI Inhibition of Cancer Cell Growth by Ruthenium(II) Arene Complexes  
AU Morris, Robert E.; Aird, Rhona E.; Murdoch, Piedad del Socorro; Chen, Haimei; Cummings, Jeff; Hughes, Nathan D.; Parsons, Simon; Parkin, Andrew; Boyd, Gary; Jodrell, Duncan I.; Sadler, Peter J.  
CS Department of Chemistry, University of Edinburgh, Edinburgh, EH9 3JJ, UK  
SO Journal of Medicinal Chemistry (2001), 44(22), 3616-3621  
CODEN: JMCMAR; ISSN: 0022-2623  
PB American Chemical Society  
DT Journal  
LA English  
AB Inhibition of the growth of the human ovarian cancer cell line A2780 by organometallic ruthenium(II) complexes of the type [(η<sub>6</sub>-arene)Ru(X)(Y)(Z)], where arene is benzene or substituted benzene, X, Y, and Z are halide, acetonitrile, or isonicotinamide, or X, Y is ethylenediamine (en) or N-ethylethylenediamine, has been investigated. The x-ray crystal structures of the complexes [(η<sub>6</sub>-p-cymene)Ru(en)Cl]PF<sub>6</sub> (I), [(η<sub>6</sub>-p-cymene)RuCl<sub>2</sub>(isonicotinamide)], and [(η<sub>6</sub>-biphenyl)Ru(en)Cl]PF<sub>6</sub> are reported. They have "piano stool" geometries with η<sub>6</sub> coordination of the arene ligand. Complexes with X, Y as a chelated en ligand and Z as a monofunctional leaving group had the highest activity. Some complexes were as active as carboplatin. Hydrolysis of the reactive Ru-Cl bond in I was detected by HPLC but was suppressed by the addition of chloride ions. I binds strongly and

selectively to G bases on DNA oligonucleotides to form monofunctional adducts. No inhibition of topoisomerase I or II by complex I was detected. These chelated Ru(II) arene complexes have potential as novel metal-based anticancer agents with a mechanism of action different from that of the Ru(III) complex currently on clin. trial.

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN  
AN 2001:319903 CAPLUS  
DN 134:326632  
TI Half-sandwich ruthenium(II) compounds comprising nitrogen containing ligands for treatment of cancer  
IN Morris, Robert Edward; Sadler, Peter John; Chen, Haimei; Jodrell, Duncan  
PA The University Court, the University of Edinburgh, UK  
SO PCT Int. Appl., 36 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001030790 W: JP, US RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE	A1	20010503	WO 2000-GB4144	20001026 <--
	EP 1224192 EP 1224192 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY	A1 B1	20020724 20050831	EP 2000-971599	20001026 <--
	JP 2003512471 AT 303393 ES 2248136 US 2003023088 US 6750251 US 2004220166 US 6979681 US 2005239765	T T T3 A1 B2 A1 B2 A1	20030402 20050915 20060316 20030130 20040615 20041104 20051227 20051027	JP 2001-533142 AT 2000-971599 ES 2000-971599 US 2002-134404 US 2004-848416 US 2005-165372	20001026 <-- 20001026 20001026 20020426 <-- 20040518 20050623
PRAI	GB 1999-25274 GB 2000-16054 WO 2000-GB4144 US 2002-134404 US 2004-848416	A A W A1 A1	19991027 20000630 20001026 20020426 20040518		
OS	MARPAT 134:326632				
GI					



AB Title compds. I (R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub> = H, alkyl, -CO<sub>2</sub>R', aryl, alkylaryl, which latter two groups are optionally substituted on the aromatic ring; R' = alkyl, aryl, alkaryl; X = halo, H<sub>2</sub>O, (R')<sub>2</sub>(R'')SO, R'CO<sub>2</sub>-, (R')(R'')C:O, R'' = alkyl, aryl, alkaryl; Y = counterion; m = 0-1; q = 1-3; C' = C<sub>1-12</sub> alkylene, optionally substituted in or on the alkylene chain, bound to two A groups; p = 0-1 and r = 1 when p is 0 and r is 2 when p is 1; and A and B are: each independently N-donor nitrile ligands; or B is halo and A is an N-donor pyridine ligand, optionally substituted at one or more of the carbon atoms of the pyridine ring; or p is 0, A is NR<sub>7</sub>R<sub>8</sub> and B is NR<sub>9</sub>R<sub>10</sub>, wherein R<sub>7</sub>, R<sub>8</sub>, R<sub>9</sub> and R<sub>10</sub> independently represent H or alkyl, and A and B are linked by an alkylene chain, optionally substituted in or on the alkylene chain; or p is 1, A is NR<sub>7</sub> and B is NR<sub>9</sub>R<sub>10</sub>, wherein R<sub>7</sub>, R<sub>9</sub> and R<sub>10</sub> are as previously defined, and A and B are linked by an alkylene chain, optionally substituted) were prepared which may be used in the treatment and/or prevention of cancer.

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s 14 and py<=2003  
23916064 PY<=2003  
L7 109 L4 AND PY<=2003

=> s 17 and cancer  
307771 CANCER  
L8 4 L7 AND CANCER

=> s 18 not 16  
L9 0 L8 NOT L6